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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/513,888	02/25/2000	Carlo M. Croce	9855-30U1	6972

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AKIN, GUMP, STRAUSS, HAUER & FELD, L.L.P.
ONE COMMERCE SQUARE
2005 MARKET STREET, SUITE 2200
PHILADELPHIA, PA 19103

EXAMINER
LOEB, BRONWEN

ART UNIT	PAPER NUMBER
1636	19

DATE MAILED: 03/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/513,888	CROCE ET AL.	
	Examiner	Art Unit	
	Bronwen M. Loeb	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,24 and 100-144* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23 and 24* is/are allowed.

6)☒ Claim(s) *100-144* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 December 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: RSL Error Report & Notice to Comply.

DETAILED ACTION

This action is in response to the amendment filed 17 December 2001 in which new claims 100-144 were presented and claims 1-22, 25, 27, 30, 34-36, 41-43, 45, 47-58, 63-68, 73-75, 84, 86, 87 and 90-97 were cancelled.

Claims 23, 24 and 100-144 are pending.

Priority

1. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § (120 or 119(e)) as follows:

> The second application (which is called a continuing application) must be an application for a patent for an invention which is also disclosed in the first application (the parent or provisional application); the disclosure of the invention in the parent application and in the continuing application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. §112. See *In re Ahlbrecht*, 168 USPQ 293 (CCPA 1971).

Upon review of the specification of the parent provisional application and comparison with the specification of the present application, it is determined that the specification of parent provisional application 60/121,537 is not enabling for the use and preparation of the instantly claimed invention. The specification of the parent application does not teach or suggest an isolated polynucleotide having a sequence comprising, or a sequence substantially homologous to, at least twenty consecutive

nucleotide residues of a portion of a strand of SEQ ID No. 1 wherein the portion is selected from the group consisting of residues 1-423, residues 871-4343, residues 4365-4419, residues 4451-4473, residues 4514-6917, residues 6939-7633 and residues 7806-852. The specification teaches specific subsets of SEQ ID No. 1 which are 112-456, 1707-2510 and 4912-5550. Since the specific subsets recited in the new pending claims (residues 1-423, residues 871-4343, residues 4365-4419, residues 4451-4473, residues 4514-6917, residues 6939-7633 and residues 7806-8520 are not disclosed in the parent application and cannot be predicted from the teachings of the parent application, the parent application is not enabling for the instantly claimed invention. Thus, the requirements of the first paragraph of 35 U.S.C. §112 have not been met. Accordingly, claims 100-143 are assigned an effective filing date of 25 February 2000.

Sequence Compliance

2. Applicant submitted a paper listing and computer readable format copy of the Sequence Listing. The computer readable format however has errors as explained on the attached Raw Sequence Listing Error Report; attached also is a Notice to Comply. It is further noted that the sequences in Fig. 3B still do not have SEQ ID Nos. labeling them, either in the Figure itself or in the Brief Description of the Drawings. This problem was made of record in the Action mailed 25 April 2001. Therefore this application remains non-compliant.

Applicants are required to comply with all of the requirements of 37 CFR 1.821 through 1.825. Any response to this office action that fails to meet all of these

requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. 1.821 through 1.825 did not preclude the continued examination of the application on the merits, the results of which are communicated below.

Drawings

3. The corrected or substitute drawings were received on 17 December 2001. These drawings are not acceptable to the Examiner because Figure 5 has panels A-Q while in the as-filed specification, in the Brief Description of the Drawings on p. 17, Figure 5 is described as having panels A-P; therefore a new panel has been added. Please see below under Specification for more discussion on this matter.

4. Attention is also drawn to the attached PTO Form 948.

Specification

5. The amendment filed 17 December 2001 is objected to under 35 U.S.C. §132 because it introduces new matter into the disclosure. 35 U.S.C. §132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: in the Brief Description of the Drawing for Figure 5 (pp.17-18), a new panel, Q, has been added whereas in the as-filed specification, only panels A-P, were described. As noted in the Action mailed 25 April 2001, Figure 5 was not filed with the original specification but was deemed not necessary to understanding the invention in the Action, therefore a copy of

Figure 5, as supported by the Brief Description of the Drawings, was required. Applicant asserts that the submitted Figure 5 "does not constitute new matter as a 'substantially similar' Figure 5 is present in the US provisional application from which this case claims priority" (p. 16 in the Amendment dated 17 December 2001). First, it is noted that a non-provisional application claiming the benefit of the filing date of a US provisional application is *not* a continuation of that provisional application. Therefore, there is no assumption or requirement that the disclosure of the non-provisional is identical to the disclosure of the provisional application. See MPEP 201.07. Second, the as-filed instant specification does not incorporate by reference the disclosure of the provisional application to which it claims benefit, the substantially similar Figure 5 in the provisional application is not incorporated by reference into the instant non-provisional application. Therefore, the extra panel (which appears to be SEQ ID No. 20, presented in Figure 5P) in the now-submitted Figure 5 is new matter.

Applicant is required to cancel the new matter in the reply to this Office Action.

6. Applicant requested further information regarding the objection to a protein being called "KIAA0522" in the specification on p. 15, line 4 and p. 96, line 17 but labeled "KIA0522" in the sequence listing for SEQ ID No. 8. The Examiner apologizes for this confusion; the protein is labeled "KIA0522" in Figure 2B, not the sequence listing; Figure 2B shows, among other sequences, SEQ ID No. 8, according to the Brief Description of the Drawings on p. 15.

Claim Objections

7. Claim 140 is objected to because of the following informalities: A space is missing in the phrase "claim123". Appropriate correction is required.

8. Claim 102 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 102 does not further limit claim 100 and indeed could have embodiments that are not encompassed by claim 100 at all. For instance, a nucleotide comprising residues 424-525 of SEQ ID No.1 is encompassed by the genus claimed in claim 102 but not by the genus claimed in claim 100.

Response to Amendment

9. All of the claim rejections set forth in the Action mailed 25 April 2001 have been withdrawn in view of Applicant's cancellation of all of the pending claims (except 23 and 24).

10. New grounds of rejection, necessitated by Applicant's amendment, are presented below. In the instances where Applicant argues possible rejections of the new claims, based on the rejections of the now-cancelled claims, responses to the arguments are provided.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 118-121, 141, 142 and 144 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction of guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

The present claims are broad. Claims 118, 119 and 141 encompass a pharmaceutical composition comprising an isolated polynucleotide. Claims 120, 121 and 142 are drawn to an animal cell comprising an exogenous isolated polynucleotide. Claim 144 encompasses a kit for selecting any anti-cancer therapeutic compound for administration to a human afflicted with any cancer.

The nature of the invention is a pharmaceutical composition and a kit comprising an isolated polynucleotide reagent for assessing expression of FEZ1 in a cell and a plurality of candidate anti-cancer therapeutic compounds. A pharmaceutical

composition requires an enabled therapeutic use for the composition; since the pharmaceutical composition comprises nucleic acid, the therapeutic use is a method of gene therapy. With regard to the animal cells, the specification contemplates only ex vivo gene therapy as the use for the claimed animal cells (p. 48, line 28-p. 49, line 15). The kit claim is essentially directed to a method for selecting an anti-cancer therapeutic compound for any cancer.

An analysis of the prior art as of the effective filing date of the present application shows the complete lack of documented success for any treatment based on gene therapy. In a review on the current status of gene therapy, both Verma et al (Nature (1997) 389:239-242) and Palù et al (J. Biotechnol. (1999) 68: 1-13) state that despite hundreds of clinical trials underway, no successful outcome has been achieved. See Verma et al, p. 239, 1st paragraph; Palù et al, p. 1, Abstract. The continued, major obstacles to successful gene therapy are gene delivery and sustained expression of the gene. Regarding non-viral methods for gene delivery, Verma et al indicates that most approaches suffer from poor efficiency and transient expression of the gene (p. 239, col. 3, 2nd paragraph). Likewise, Luo et al (Nature Biotechnology (2000) 18:33-37) indicates that non-viral synthetic delivery systems are very inefficient. See p. 33, Abstract and col. 1, 1st and 2nd paragraphs. While all three references indicate the promise of gene therapy, it is still a technique of the future and advancements in our understanding of the basics of gene delivery and expression must be made before gene therapy becomes a useful technique. See Verma et al, p. 242, col. 2-3; Palù et al, pp. 10-11; Luo et al , p. 33, col. 1, 1st paragraph. With respect to FEZ1, the prior art shows a loss

of heterozygosity (LOH) in band 21-22 of human chromosome 8 in a wide range of different cancers. See, for instance, Boige et al (1997 Cancer Research 57: 1986-1990); El-Naggar et l (1998 Oncogene 16: 2983-2987); and Anbazhagan et al (1998 Am. J. Pathology 152: 815-819). Putative tumor suppressor genes have been identified in this chromosomal region; their role has not been definitively established. The prior art further suggests that a wide range of LOH's may be associated with a particular disease, which may correlate to the genetic complexity underlying these cancers. See Kerangueven et al (1997 Cancer Research 57: 5469-5474). As additional evidence of the complexity of cancer, and the unpredictable nature regarding its cause and progression, chromosome 8 complementation in different colorectal cancer cell lines has different responses, indicating the role of unknown other genetic mutations in these various cell lines. See Gustafson et al (1996 Cancer Research 56: 5238-5245). No prior art teaches definitive evidence of the role of expression of the FEZ1 gene and any cancer.

The relative skill of those in the art of gene therapy, cancer and cancer therapeutics is high.

The area of the invention is unpredictable. The fundamental mechanism of disease has been determined for very few cancers, therefore one is unable to model what specific types of compounds will be therapeutic for any particular cancer. Since the role of FEZ1 expression has not been established in any cancer, there is no factual basis on which to model predictions about the therapeutic nature of compounds. In a given cancer type, there can be a wide range of diversity in the genetic basis of the

disorder, rendering accurate prediction even less possible. Therefore, there is little more than extensive trial and error available to assess which compounds among those that affect expression of the FEZ1 gene are likely to be therapeutic for the wide range of cancers disclosed. As discussed above for gene therapy, the method of in vivo or ex vivo gene therapy is highly complex and unpredictable. Indeed, the recent tragic and unexpected death of a participant in a gene therapy clinical trial clearly illustrates the unpredictable nature of gene therapy. See Fox, ASM News, Feb. 2000, 66 (2): 1-3. The skilled artisan at the time the present invention was made recognized the difficulty of achieving sufficient heterologous gene expression to induce any therapeutic effect.

The present specification provides little direction of guidance to support the claimed invention. There is no direction provided as to how to overcome the obstacle to gene therapy recognized by leaders in the field, i.e. low efficiency of gene delivery and transient gene expression. The specification generally discloses the use of the kit for a very broad group of cancers, and disorders including tubulin hyperpolymerization disorders and tubulin hypopolymerization disorders. The specification discloses a correlation between FEZ1 expression and some different primary tumors, or cell lines. The specification does not disclose the statistical significance of the data, or establish whether FEZ1 expression is a causal factor in any particular cancer. Methods of assessing the effect of a compound on the expression of a gene are well known in the art. However, the specification provides no direction as to how to predict which compounds among those that affect expression of the FEZ1 gene are likely to be therapeutic.

No working examples are disclosed which are encompassed by the claim.

The quantity of experimentation necessary to carry out the claimed invention is high, as the skilled artisan could not rely on the prior art or the present specification to teach how to use the claimed pharmaceutical compositions or the kit. In order to determine how to use the pharmaceutical composition to treat a condition, one of skill in the art would have to determine what effect exogenous transgene expression would have in any cell type, whether the effect could be exploited for treatment of a disease, how to deliver the given nucleic acid to the appropriate target cells with specificity and efficiency, and how to get sufficient expression to induce at least some therapeutic effect. In order to determine how to use the claimed kit for selecting an anti-cancer therapeutic compound, one of skill in the art would have to determine if FEZ1 expression was fundamentally related to the disease mechanism for any given disease, and then would have to determine the therapeutic capacity of any compound shown to affect FEZ1 expression. Since neither the prior art nor the specification provides the answers to these questions, one of skill in the art would have to undertake a large quantity of trial and error experimentation to answer them.

Based on the broad scope of the claims, the unpredictability in the area of the invention, the lack of sufficient guidance or working examples in the specification and the quantity of experimentation necessary, it would clearly require undue experimentation by one of skill in the art to determine how to use the claimed pharmaceutical compositions in gene therapy or kit for selecting an anti-cancer therapeutic compound for administration to a human afflicted with a cancer.

With respect to the enablement of the claimed kit, Applicant argues that "it is not necessary that a skilled person understand how a given candidate anti-cancer therapeutic compound affects expression of FEZ1 but only how such a candidate anti-cancer therapeutic compound may affect the cancer for which the assessment of expression of FEZ1 in a cell provides information". The Examiner agrees with this statement completely. The claimed kit comprises a plurality of candidate anti-cancer therapeutic compounds and a polynucleotide reagent for assessing FEZ1 expression. The problem is, as set forth in the Action dated 25 April 2001, the role of FEZ1 expression has *not* been established in any cancer. In other words, the assessment of FEZ1 expression in any particular cancer does not in fact provide information at all about whether a compound identified as affecting FEZ1 expression would have a therapeutic impact on any cancer. Applicant's argument does not overcome the rejection.

The rejection of claim 144 may be overcome by amending the claim to recite "A kit for identifying

13. Claims 100-143 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Amended claim 100 is drawn to an isolated nucleic acid molecule having a sequence comprising at least twenty consecutive nucleotide residues of a portion of a strand of SEQ ID No. 1 wherein the portion is selected from the group consisting of

residues 1-423, residues 871-4343, residues 4365-4419, residues 4451-4473, residues 4514-6917, residues 6939-7633 and residues 7806-8520. Claim 123 is drawn to an isolated polynucleotide having a sequence that is substantially homologous with twenty consecutive nucleotide residues of a portion of SEQ ID No.1 wherein the portion is selected from the group consisting of residues 1 -423, residues 871-4343, residues 4365-4419, residues 4451-4473, residues 4514-6917, residues 6939-7633 and residues 7806-8520. While the specification teaches portions of SEQ ID No. 1 including 112-456, 1707-2510 and 4912-5550, it does not teach or suggest any of the other specific subsets recited in claims 100 and 123. The recitation of these specific subsets (residues 1-423, residues 871-4343, residues 4365-4419, residues 4451-4473, residues 4514-6917, residues 6939-7633 and residues 7806-8520) is therefore deemed to be new matter and must be removed from the claims. This is a NEW MATTER rejection.

14. The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. It is noted that with respect to the use of "having" or "has", Applicant has stated on the record these words are closed when used with an isolated nucleotide. See p. 20 of the Amendment filed 17 December 2001.

16. Claims 100-122, 126-132, 135 and 136 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 100 is vague and indefinite in reciting "at least twenty consecutive nucleotide residues of a portion" and "the portion includes a residue selected from the

group..". It is unclear how the isolated polynucleotide can satisfy both of these limitations, thus the metes and bounds of the claim are unclear.

Claim 100 is vague and indefinite in reciting "residues 6939 and 7633". Is the "and" supposed to be "to" or does the portion comprise these two residues?

Claims 112, 113, 135 and 136 are vague and indefinite in reciting "an immobilized polynucleotide" as a member of the Markush group of detectably labeled isolated polynucleotides. Applicant argues that the specification makes clear that an immobilized polynucleotide is a detectably labeled isolated polynucleotide as it permits the detection of a desired polynucleotide. Applicant points to p. 29, lines 5-6 as a definition. These arguments are not persuasive. First, the specification was reviewed prior to making this rejection in the Action dated 25 April 2001. Second, the complete definition is on lines 4-6 on p. 29. "A protein or polynucleotide is "detectably labeled" if the protein or polynucleotide comprises or is linked with a composition of matter which can be detected after contacting the protein or polynucleotide with another protein or polynucleotide." In other words, the composition of matter is what is detected after the contacting. In the case of the immobilized polynucleotide, for instance on a gene chip, the composition of matter to be detected is the gene chip. It is unclear how detecting the gene chip is comparable to detecting a ligand label, for instance, in a protein-ligand pair.

Claim 126 is vague and indefinite as it is unclear how a twenty residue isolated polynucleotide can comprise the three recited subsets of SEQ ID No.1 which total well over twenty nucleotides.

Claim 127 is vague and indefinite as it is unclear how a twenty residue isolated polynucleotide can comprise the sequence of SEQ ID No. 3 which is 1791 nucleotides.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

18. Claims 100, 110-112, 113, 123 and 133-135 are rejected under 35 U.S.C. 102(e) as being anticipated by Chader et al (USP 5,840,686). Chader et al teach an isolated nucleic acid (SEQ ID No. 11) comprising a sequence identical to residues 7126-7147 of SEQ ID No. 1. The isolated polynucleotide was cloned into a nucleic acid vector (PT7 Blue vector). The isolated nucleic acid was detectably labeled using a fluorescent label for fluorescent sequencing. See SEQ ID No. 11, col. 2, lines 41-43, col. 18, lines 64-67 and col. 19, line 1-col. 20, line 29.

19. Claims 100-104, 110-112, 114, 122-127, 132-135, 137 and 143 are rejected under 35 U.S.C. 102(a) as being anticipated by Ishii et al (Proc Natl Acad Sci (1999) 96:3928-3933). Ishii et al teach SEQ ID No. 1. Pairs of primers for exons 1-3 were labeled for use in sequencing. Sequences were contained in yeast artificial chromosomes and bacterial artificial chromosomes. Substantially purified nucleic acids are taught (Northern blots; sequencing gel). See entire document.

Applicant submitted a declaration under 37 CFR 1.132 to remove the Ishii et al reference as prior art. This is not persuasive as the declaration was unsigned.

Conclusion

Claims 23 and 24 are allowed. Claims 100-144 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from 10:00 AM to 6:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, can be reached on (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to Tracey Johnson, Patent Analyst whose telephone number is (703) 305-2982.

Bronwen M. Loeb, Ph.D.
Patent Examiner
Art Unit 1636

March 10, 2002

Remy Yucel

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Notice to Comply	Application No.	Applicant(s)	
	09/513,888	CROCE ET AL.	
	Examiner	Art Unit	
	Bronwen M. Loeb	1636	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☒ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
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